ABSTRACTS

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Circulating Endothelial Progenitor Cells in Cardiovascular Outcomes

Werner N, Kosiol S, Schiegle T, et al. N Engl J Med 2005;353:99-1007.

Conclusion: Endothelial progenitor cells positive for CD-34 and kinase domain receptor (KDR) predict occurrence of death from cardiovascular causes and cardiovascular events.

Summary: Endothelial progenitor cells can differentiate into endothelial cells and proliferate. They may be candidates for mediating vascular regeneration. These cells, derived from the bone marrow, are thought to support vascular endothelium integrity. Levels of endothelial progenitor cells correlate inversely with cardiovascular risk factors. The authors sought to study the prognostic value associated with circulating endothelial progenitor cells.

Endothelial progenitor cells positive for CD-34 and KDR were determined using flow cytometry. Five hundred and nineteen patients with coronary artery disease confirmed by angiography were studied. After twelve months of follow-up, association between death from cardiovascular causes, the occurrence of a first major cardiovascular event (defined as myocardial infarction, hospitalization, revascularization, or death from cardiovascular cause), revascularization, hospitalization, and death from all causes was correlated with baseline levels of endothelial progenitor cells.

Two hundred and fourteen patients had a first major cardiovascular event, 43 participants died, with 23 of these deaths from cardiovascular causes. Adjusting for age, vascular risk factors, sex, and other variables relevant to cardiovascular disease, increased levels of endothelial progenitor cells were associated with a reduced risk of a first major cardiovascular event (Hazard ratio (HR) 0.74; 95% confidence interval (CI) 0.62 to 0.89; $P = .002$), death from cardiovascular causes, (HR 0.31; 95% CI 0.16 to 0.63; $P = .001$), hospitalization (HR 0.76; 95% CI 0.63 to 0.94; $P = .01$), and revascularization (HR 0.77; 95% CI 0.62 to 0.95; $P = .02$). Myocardial infarction and death from all causes were not predicted by endothelial progenitor-cell levels.

Comment: The role of endothelial progenitor cells in rejuvenation of vascular endothelium is currently an area of intensive investigation. It appears these immature cells may modify the pathogenesis of atherosclerotic disease. Measurement of endothelial progenitor cells may improve risk stratification in patients with cardiovascular disease.

Evaluation of the Safety and Effectiveness of Renal Artery Stenting After Unsuccessful Balloon Angioplasty: The ASPIRE-2 Study

Rocha-Singh K, Jaff MR, Rosenfield K, and the ASPIRE-2 Trial Investigators. J Am Coll Cardiol 2005;46:776-83.

Conclusion: Balloon-expandable stents in hypertensive patients with ostial renal artery atherosclerotic stenosis can have a beneficial impact on hypertension when initial transluminal angioplasty is unsuccessful.

Summary: The authors sought to define safety and durability of renal artery stents following suboptimal or failed renal artery angioplasty when renal vascular hypertension was suspected. This was a non randomized study that enrolled 208 patients with either primary or restenontic (>70%) ostial renal artery stenosis. All patients underwent placement of a balloon-expandable stent following an unsuccessful transluminal angioplasty. Unsuccessful transluminal renal artery angioplasty was defined as >50% residual stenosis, flow limiting dissection, or a persistent trans-lesion pressure gradient. Primary end point was restenosis at 9 months as determined by angiogram or duplex scanning. Secondary end points included blood pressure, cumulative adverse events, renal function, and target lesion revascularization at 24 months.

In 80.2% of cases, placement of the stent was immediately successful (n = 182 of 227). Nine month restensosis rate was 17.4%. Systolic blood pressure decreased from 168 ± 25 mm/Hg at baseline to 149 ± 24 mm/Hg at 9 months and 149 ± 25 mm/Hg at 24 months ($P < .001$). At 24 months, the cumulative rate of major adverse events was 19.7%. Serum creatinine concentrations were unchanged from baseline values at both 9 and 24 months.

Comment: The study is limited by its retrospective nature and lack of controls in that no patients were treated with medical therapy or simple balloon angioplasty alone. In addition, primary stenting of renal artery ostial lesions is currently routine. The study provides reasonable information regarding recurrent stenosis in a sub group of patients undergoing renal artery stenting. Overall, however, it is of little relevance to modern practice.

Risk of Major Haemorrhage in Patients After Infra-Inguinal Venous Bypass Surgery: Therapeutic Consequences. The Dutch BOA (Bypass Oral Anticoagulants or Aspirin) Study

Ariesen NJ, Tangelder MJD, Lawson JA, and the Dutch Bypass Oral Anticoagulants or Aspirin (BOA) Study. Eur J Vasc Endo Surg 2005;30: 154-159.

Conclusion: Even considering the risk of hemorrhage, it is recommended patients following peripheral venous bypass surgery be routinely treated with oral anticoagulants.

Summary: The Dutch Bypass Oral Anticoagulants or Aspirin (BOA) study indicated oral anticoagulants were more effective than aspirin in preventing occlusion of lower extremity vein bypass grafts (Hazard Ratio) 0.69, 95% CI 0.54-0.88. Lancet 2000;355:1186-1187). In the BOA study, however, there was two-fold increase risk of bleeding complications in patients treated with oral anticoagulants following peripheral bypass surgery (HR 1.96, 95% CI 1.42-2.71). In this study, the authors developed a model to identify patients treated with anticoagulation who are at risk of major hemorrhage. They also included in their model an estimation of whether hemorrhage could be prevented by the use of aspirin rather than by the use of oral anticoagulants.

Data of patients in the BOA study was reanalyzed with Cox regression techniques. In the BOA study, there were 1,326 patients randomized to oral anticoagulants and 1,324 randomized to aspirin.

There was an increased risk of major hemorrhage in patients on anticoagulants associated with systolic blood pressure greater than 140 mm/Hg (HR 1.62), diabetes mellitus (HR 1.60), and age ≥75 years (HR 2.77). Stratifying patients according to risks quartiles; if patients in the highest risk quartile had received aspirin rather than anticoagulants, the number of patients with major hemorrhage would, according to the model, have been reduced from 46 to 22. This would have been associated with no major changes in ischemic events or graft occlusions. In the subgroup of patients with venous bypasses, a similar analysis indicated major hemorrhages would be reduced from 27 to 13 patients, but at a cost of 7 more mostly fatal ischemic events and 17 more graft occlusions.

Comment: The BOA study is widely known and widely quoted but thus far its findings have had little influence on the treatment of patients with peripheral vein bypass grafts. Part of the lack of acceptance of the BOA recommendations undoubtedly has to do with the increased hemorrhage rate with the use of anticoagulants. This analysis suggests that even with the increased hemorrhage rates using oral anticoagulants, patients with vein bypasses still benefit overall with oral anticoagulants compared to aspirin. Although the authors' model is interesting, this type of retrospective analysis, in itself, is not going to convince many to utilize oral anticoagulants as routine prophylaxis against vein bypass graft occlusion.

Is Duplex Surveillance of Value After Leg Vein Bypass Grafting? The Principle Results of the Vein Graft Surveillance Randomized Trial (VGST)

Davies AH, Howdon AG, Thompson SG, and the VGST Participants. Circulation 2005;112:1985-991.

Conclusion: Intensive postoperative graft surveillance with duplex scanning following lower extremity vein bypass graft operations does not result in lower amputation rates than a simple program of clinical surveillance.

Summary: This was a multicenter, randomized, prospective, controlled clinical trial. There were 594 patients with a patent vein graft 30 days following surgery. These patients were randomized to either clinical follow up alone or a duplex follow up program with studies at 6 weeks and then 3, 6, 9, 12, and 18 months postoperatively. Approximately 2/3 of the grafts were placed for critical ischemia with 2/3 of the distal anastomoses to the popliteal artery either above or below the knee. Approximately 1/3 of the patients in each group had diabetes and the median age was 70 years in each group. Ipsilateral greater saphenous vein was used in 92% of the clinical follow up group and 94% of the duplex follow up group.

There are no differences in the clinical and duplex surveillance groups with respect to amputation rates (7% for each group) or vascular mortality (3% v 4%) at 18 months. There were more stenoses at 18 months in the clinical group (19% v 12% $P = .04$). Primary patency, primary assisted patency, and secondary patency were similar in the clinical group (69%, 75%, and 80% and the duplex group 67%, 76%, and 79%). There were no apparent